Light at the end of the tunnel

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In the early stages of developing the antiviral drug, Huan, Awang and their team of researchers toiled in a small lab in Tawau where they experienced power cuts three times a week, which brought their work to a sudden and complete halt. "We would be in the middle of something and everything would stop – the PCR machine, fridge, and air-cond. It was a complete black-out."

Things took a turn for the better when they received a RM1.37 million grant from the Ministry of Science Technology and Innovation to upscale their efforts and shift their lab to Kota Kinabalu, Sabah. By then, they had formed two full scale biotechnology companies namely Defensia Sdn Bhd and BioSatria Sdn Bhd. The lack of internet options at their new premise allowed for smoother progress and not long after, the team began testing their oral delivery antiviral fusion protein called RetroMAD1 on prawns that were experimentally infected with WSSV. The survival rate for prawns fed with RetroMAD1 was 100 per cent, while an untreated batch also infected with WSSV had a 100 per cent mortality rate.

The promising results motivated Huan and Awang to explore the prospect of testing the drug on HIV-1 patients. "Don't forget, we designed our drug based on 'HIV-1,'" Huan points out. However, when he approached a number of people involved in HIV-1 research, the responses he received were tepid. The reactions were along the lines of "how can a prawn drug be used for HIV-1?" He continues, "It doesn't make sense so we didn't make any headway at all."

However, he was not ready to throw in the towel. "I thought okay, if we cannot test on HIV-1, then we will test on the virus nearest to HIV-1, which is FIV."

Dr Benny Tan and Orange.

CURING CATS AND DOGS: Enter Dr Tan, who was introduced to Huan by a mutual friend. "When Huan came into the picture, I said, 'I'm glad to try it, I've got the perfect candidate for you,'" remembers the affable veterinarian with a laugh.

At that time, it had been about four months since Orange had been diagnosed with FIV. Dr Tan, who by then had claimed ownership of the cat, didn't have the heart to put Orange down. So, he decided to only do so when the cat's health deteriorated to a stage where it became necessary.

But then, hope emerged in the form of an unassuming looking liquid – clear like water, tasteless and free of any odour. Orange was the first cat to be treated with RetroMAD1.

"Within the first two or three weeks, I noticed the ulcers had shrunk," recalls Dr Tan amidst the cacophony of barking dogs and meowing cats at his clinic. "Once we started him on RetroMAD1, it took him two to three months to completely heal. By completely heal, I mean all the ulcers were gone and his skin was there."

The next test subject at Dr Tan's clinic was a tiny puppy that had contracted the parvovirus. "This virus is very acute and severe. You will see dogs vomiting. Small guys that weigh below one to two kilogrammes don't stand a chance."

Yet, the 700g puppy who was fed RetroMAD1 survived. Dr Tan was cautiously elated by the outcome. "I thought, wow, there is something about this drug. It really works but this was just two animals, it may just be a coincidence."

> "What makes it effective is that it acts from three different stages. If it fails in the first stage, it has three more stages to act on the virus."
> *Dr Benny Tan*

Since then, he has had over 40 successful cases of cats and dogs treated with RetroMAD1. He attributes the high success rate of the drug to its broad spectrum approach. "What makes it effective is that it acts from three different stages. If it fails in the first stage, it has three more stages to act on the virus."

However, the success rate is not 100 per cent. The drug was not successful in treating pets infected by the Canine Distemper Virus (CDV) and the Feline Infectious Peritonitis Virus (FIPV), says Dr Tan.

According to him, RetroMAD1 showed the most promise with parvovirus where test results indicated there were no signs of the virus at all after recovery. In the case of FIV and Feline Leukemia Virus (FeLV), the cats are clinically cured and back to their normal selves but the virus is not completely gone. "In a lot of cases, if you recover from viral infection, the virus does hide somewhere in your body. Not in its full form but part of it is there," explains Dr Tan. "Those with FIV and FeLV may need lifelong treatment of RetroMAD1."

This includes Orange who was first treated with RetroMAD1 somewhere towards the end of 2009. Today, the former stray lives happily in Dr Tan's clinic where he appears none the worse for wear – a friendly feline full of energy and enthusiasm.

Last year, a veterinarian in Batu Pahat, Johor, Dr Mohanakrishnan began testing RetroMAD1 on his patients. In his 25 years of practice, Dr Mohanakrishnan says he had yet to come across a drug that could reverse the damage done by viruses. Between October and December, he treated a combination of 16 cats and dogs for various diseases including the parvovirus, canine coronavirus, calicivirus and FeLV with RetroMAD1. Out of the 16, there were four fatalities. "Twelve out of 16 is not bad," maintains Dr Mohanakrishnan in a phone interview, who adds that pet owners should vaccinate their companion animals to avoid viral infection in the first place.

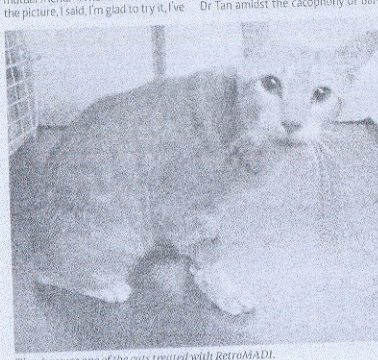
Dr Tan and Dr Mohanakrishnan's clinics are participants of the multicentre anecdotal trials being conducted to get RetroMAD1 ready for the Malaysian market. Huan and his team are also researching potential companion animal markets worldwide. "We are already exploring the top 10 cat and dog population areas of the world," he elaborates, adding that penetrating the global market will take time as they would have to fulfil the regulatory requirements of various countries.

With the support of a group of investors who want to see a local drug do well at the international level, BioValence Sdn Bhd was formed to upscale production and commercialisation of RetroMAD1 for the global market. Huan was appointed Chief Technology Officer of the company and Professor Shamala Devi, a leading Malaysian virologist was appointed Chief Science Officer. BioValence will soon have its own GMP compliant animal drug manufacturing facility in Taman Mayang, Petaling Jaya, Selangor, while another cGMP/USFDA compliant clinical batch plant is on the drawing board with submissions being presented to the National Pharmaceutical Control Bureau.

GOING GLOBAL: RetroMAD1 will begin its venture to international shores in the aquaculture industry as the regulatory requirements are not as stringent compared to that of companion animals. "For aquaculture, it either works or it doesn't. Unlike with antibiotics, there is no bioaccumulation risk with our drug because it is a protein," explains Huan. "So in terms of a food fish or a food prawn, it would be very easy in terms of regulatories, both here and worldwide."

The effort to go global got a shot in the arm when BioValence formed a strategic alliance with INVE Aquaculture, a multinational company headquartered in Belgium, to distribute RetroMAD1 globally for aquaculture use. "The Managing Director of INVE, Dr Philippe Leger, told me that all of INVE's products to date are their own. RetroMAD1 will be the first product they are selling that is not their own," enthuses Huan. "INVE has got 25 years of experience and 1,500 corporate clients in 70 nations. So, they would be our main business conduit, at least in the initial stages, for RetroMAD1 in aquaculture application."

AIMING TO SAVE LIVES: While they have made advancements in developing the drug for animal application, Huan, Awang and Professor Shamala still have their eyes on the main prize, which is to fulfil RetroMAD1's potential for human use. Preliminary tests have been conducted to explore its efficacy in treating dengue, oral and genital herpes, and Rotavirus. "The antiviral business is valued at US$28 billion (RM85 billion) every year. Viruses are, by and large, still a threat to humankind," maintains Huan. "I think the most challenging thing in the future for us would be saving lives. We hope to find a cure for HIV one day and it will all be worth it. It's not every day someone is given the opportunity to save a human life or help prevent a major viral outbreak."



Tigerboy was one of the cats treated with RetroMAD1.